

Abstract

KUŽMOVÁ, Darina. *Investigations of the effects of plasma activated liquids to normal and cancerous cells and 3D tumour models using molecular methods* [Dissertation thesis]. Department of astronomy, physics of the Earth and meteorology. Faculty of mathematics, physics and informatics. Comenius University, Bratislava. Supervisor: prof. RNDr. Zdenko Machala, DrSc. Consultant: doc. Ing. Helena Gbelcová, Ph.D., Bratislava: FMFI UK, 2026.

Oncological treatments face a critical challenge represented by acquired tumor chemoresistance and the toxicity of conventional therapeutics. Innovative therapy utilizing cold plasma presents a significant potential, especially for patients who do not respond positively to the conventional therapy.

The presented study investigates the therapeutic potential of indirect application of cold atmospheric plasma through plasma-activated phosphate-buffered saline (PAPBS), focusing on the physicochemical characterization of PAPBS and the validation of its antitumor efficacy and application safety on advanced 2D and 3D cell and tissue models.

Plasma activation of PBS via a positive streamer corona discharge demonstrated the successful generation of RONS, quantitatively linearly dependent on the plasma activation time, without altering the acidity of the solution.

Biological efficacy and selectivity were evaluated on human prostate adenocarcinoma cell lines (PC-3) and non-cancerous prostate cells (WPMY-1). Results in 2D conditions confirmed a significant selective effect on malignant cells while simultaneously maintaining a higher resistance of non-cancerous prostate cells.

Testing the effect of PAPBS on the paclitaxel-sensitive human breast adenocarcinoma cell line MCF-7 and its paclitaxel-resistant subline MCF-7/PAX demonstrated not only a potent antitumor effect but also the ability to overcome the tumor chemoresistance. A breakthrough finding is the high sensitivity of specifically resistant 3D spheroids (MCF-7/PAX) to PAPBS treatment. While low plasma doses induced beneficial spheroid shrinkage, higher doses were accompanied by massive disruption of intercellular adhesion and the subsequent collapse of the 3D spheroid structure and the tumor viability.

In addition to therapeutic efficacy, application safety is a key aspect. Tests on a dermal tissue model, EpiDerm™, clearly excluded any irritant effect of PAPBS on healthy skin, thereby confirming the biocompatibility of PAPBS.

The research was extended to evaluate the effect of PAPBS on a complex skin tissue model with incorporated melanoma cells simulating early-stage disease, allowing for monitoring of the impact of PAPBS on melanoma progression over time. Although immediate metabolic tests on the melanoma skin model did not show a decrease in overall viability, definitive confirmation of the inhibitory effect will be provided by the ongoing histological analysis from the 14-day observation period.

The presented study confirms that PAPBS is a sufficiently stable and selective potential antitumor drug candidate, capable of eliminating chemoresistant tumors while remaining safe upon contact with healthy skin. PAPBS could represent an effective strategy for neoadjuvant therapy. With plasma dose optimization, PAPBS therapy could lead to the complete eradication of the tumor site, as well as serve in the treatment of chronic oncological wounds.

Keywords: cold plasma, plasma activated liquids, cancer, spheroids, chemoresistance